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Supplemental Material

Bisphenol A and Reproductive Health: Update of Experimental and Human Evidence, 2007–2013

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Table S1. BPA, ovarian and oviductal outcomes, and steroidogenesis in experimental studies.

Source	Animal	Strain	Exposure route	Time of exposure	Doses	Age at collection	Outcome
Adewale et al. 2009	Rat	Long-Evans	Subcutaneous injection	Neonatal exposure: PNDO-PND3	50µg/kg and 50mg/kg	PND148	Disrupted ovarian development
Berger et al. 2008	Mouse	CF-1	Subcutaneous injection	Gestational exposure: GD1-GD4	0.01-300mg/kg	GD6	Decreased number of implantation sites, decreased progesterone
Berger et al. 2008	Mouse	CF-1	Subcutaneous injection	Gestational exposure: GD0,1, or 2	200 and 300mg/kg	GD6	Decreased number of implantation sites, decreased progesterone
Berger et al. 2010	Mouse	CF-1	Subcutaneous injection	Gestational exposure: GD1-GD4	100, 200, 300mg/kg	GD6	Altered estrogen receptor and progesterone gene expression
Brieño-Enriquez et al. 2011a	Human	NA	*In vitro*; Fetal oocytes	7, 14, 21 days	1, 5, 10, 20, 30µM	18-22 weeks old	Oocyte degeneration, impaired meiosis
Brieño-Enriquez et al. 2011b	Human	NA	*In vitro*; Fetal oocytes	7, 14, 21 days	30µM	18- 22 weeks old	Increased oocyte DNA double strand break, signaling, and repair genes
Chao et al. 2012	Mouse	CD-1	Subcutaneous injection	Neonatal exposure: PND7-PND14	20, 40µg/kg	PND15	Impaired methylation of imprinted genes during oogenesis, increases primordial follicular recruitment
Chao et al. 2012	Mouse	CD-1	Subcutaneous injection	Neonatal exposure: PND5,10,15,20	20, 40µg/kg	PND21	Impaired methylation of imprinted genes during oogenesis, increases primordial follicular recruitment
Eichenlaub-Ritter et al. 2008	Mouse	MF1	*In vitro*; Prepubertal oocytes	16 hours	0.22-43.8µM	After culture	Impaired meiosis, increased meiotic arrest, normal GVBD
Eichenlaub-Ritter et al. 2008	Mouse	MF1	Oral gavage	Neonatal exposure: PND22-PND28	20, 40, 100ng/g	PND28	Impaired meiosis, increased meiotic arrest, normal GVBD

Source	Animal	Strain	Exposure route	Time of exposure	Doses	Age at collection	Outcome
Fernandez et al. 2010	Rat	Sprague-Dawley	Subcutaneous injection	Neonatal exposure: PND1-PND10	5µg/50µL, 50µg/50µL, 500µg/50µL	4-5 months old	Increased testosterone and estradiol, increased follicular cysts, increased infertility
Grasseli et al. 2010	Pig	NA	*In vitro*, granulosa cells	48 hours	0, 0.1, 1, 10µM	NA	Altered steroidogenesis, increased VEGF
Hunt et al. 2012	Non-human primate	Rhesus macaque	Dietary exposure	Gestational exposure: GD50-GD100	400µg/kg	GD100	Impaired meiosis, increased multi-oocyte follicles, increased unenclosed and non-growing oocytes
Hunt et al. 2012	Non-human primate	Rhesus macaque	Dietary exposure	Gestational exposure: GD100-term	400µg/kg	PND0	Impaired meiosis, increased multi-oocyte follicles, increased unenclosed and non-growing oocytes
Hunt et al. 2012	Non-human primate	Rhesus macaque	Silastic pump	Gestational exposure: GD50-GD100	2.2-3.3ng/mL serum levels	GD100	Impaired meiosis, increased multi-oocyte follicles, increased unenclosed and non-growing oocytes
Hunt et al. 2012	Non-human primate	Rhesus macaque	Silastic pump	Gestational exposure: GD100-term	2.2-3.3ng/mL serum levels	PND0	Impaired meiosis, increased multi-oocyte follicles, increased unenclosed and non-growing oocytes
Kobayashi et al. 2012	Rat	Sprague-Dawley	Dietary exposure	Gestational and neonatal exposure: GD6-PND21	0, 0,33, 3,3, and 33 ppm	5 weeks or 3 months old	No change in hormones, AGD, lower ovarian weight
Lawson et al. 2011	Mouse	C57BL/6	Oral exposure	Gestational exposure: GD11-GD14.5	20ng/g	GD12, 12.5, 13.5, 14.5	Disrupted oogenesis via meiotic gene expression alterations
Lee SG et al. 2013	Rat	Sprague-Dawley	Oral gavage	Postnatal exposure: 90 days	0.001 and 0.1mg/kg	21 weeks old	Decreased testosterone and estradiol, increased atresia
Lenie et al. 2008	Mouse	C57BL/6j x CBA/Ca	*In vitro*: Early preantral follicles	12 days	3nM-30µM	NA	Impaired meiosis, impaired follicle development
Li Y et al. 2013	Rat	Wistar	Intraperitoneal injection	Neonatal exposure: 7 days	10, 40, 160mg/kg	35 days old	Decreased follicle numbers, increased atretic follicles

Source	Animal	Strain	Exposure route	Time of exposure	Doses	Age at collection	Outcome
Machtinger et al. 2013	Human	NA	*In vitro*: Adult oocytes	30 hours	20, 200ng/ml, 20μg/ml	Immature (GV stage) oocytes	Increased meiotic arrest, disrupted spindle formation and chromosome alignment, increased spontaneous oocyte activation
Mendoza-Rodriquez et al. 2011	Rat	Wistar	Drinking water	Gestational and neonatal exposure: GD6-PND21	10mg/L (1.2mg/kg)	7 weeks old	Increased uterine epithelial and stromal thickness, decreased uterine epithelial apoptosis, downregulation of *Esr1* expression in epithelial cells
Newbold et al. 2009	Mouse	CD-1	Subcutaneous injection	Gestational exposure: GD9-GD16	0, 0.1, 1, 10, 100, 1000μg/kg	18 months old	Induced ovarian cyst-adenomas, induced progressive proliferative oviductal lesions
Pacchierotti et al. 2008	Mouse	C57BL/6	Oral gavage	Postnatal exposure: Single dose	0.2 and 20mg/kg	4-11 weeks old	No effect on meiotic abnormalities
Pacchierotti et al. 2008	Mouse	C57BL/6	Oral gavage	Postnatal exposure: Single dose	0.04mg/kg	4-11 weeks old	No effect on meiotic abnormalities
Pacchierotti et al. 2008	Mouse	C57BL/6	Drinking water	Postnatal exposure: 7 weeks	0.5mg/L	4-11 weeks old	No effect on meiotic abnormalities
Peretz et al. 2012	Mouse	CD-1	*In vitro*:Antral follicles	24-96 hours	4.4-440μM	32-35 day old mice	Inhibited follicle growth, induced atresia, dysregulated cell cycle
Peretz et al. 2011	Mouse	FVB	*In vitro*:Antral follicles	24-120 hours	4.4-440μM	32-35 day old mice	Inhibited follicle growth, inhibited steroidogenesis
Rivera et al. 2011	Lamb	Hampshire Down	Subcutaneous injection	Neonatal exposure: PND1-PND14	50μg/kg	PND1, 5, 10, 30	Increased primordial follicular recruitment, increased multi-oocyte follicles, increased granulosa and theca cell proliferation, induced atresia
Rodríguez et al. 2010	Rat	Wistar	Subcutaneous injection	Neonatal exposure: PND1-PND7	0.05 and 20mg/kg	PND8	Increased primordial follicular recruitment, increased granulosa cell proliferation
Signorile et al. 2010	Mouse	Balb-c	Subcutaneous injection	Gestational exposure: GD1-PND7	100 and 1000μg/kg	3 months old	Induced endometriosis-like phenotype

Source	Animal	Strain	Exposure route	Time of exposure	Doses	Age at collection	Outcome
Tan et al. 2013	Mouse	ICR	Oral gavage	Gestational exposure: E13-E16	2, 20, 200mg/kg	E17	Increased estradiol, testosterone, and corticotropin releasing hormone
Trapphoff et al. 2013	Mouse	C57BL/6x CBA/Ca	*In vitro*: Pre-antral follicles	12 days	3 and 300nM	12-14 days old	Accelerated follicle development, disrupted genomic imprinting
Varayoud et al. 2011	Rat	Wistar	Subcutaneous injection	Neonatal exposure: PND1, 3, 5, and 7	0.05 and 20mg/kg	F1: GD5 or GD18	Down-regulated estrogen receptor and progesterone receptor
Veiga-Lopez et al. 2013	Lamb	Suffolk	Subcutaneous injection	Gestational exposure: GD30-GD90	0.5mg/kg	GD60 and GD90	Altered steroidogenic and miRNA gene expression
Xi et al. 2011	Mouse	CD-1	Oral gavage	Postnatal exposure, F0: GD1-PND20	12, 25, 50mg/kg	PND50	Disrupted feedback circuits of hypothalamic-pituitary-gonad axis
Xi et al. 2011	Mouse	CD-1	Oral gavage	Postnatal exposure, F1: PND21-PND49	12, 25, 50mg/kg	PND50	Disrupted feedback circuits of hypothalamic-pituitary-gonad axis
Xi et al. 2011	Mouse	CD-1	Oral gavage	Postnatal exposure, F1: PND21-PND49	25 and 50mg/kg	PND50	Disrupted feedback circuits of hypothalamic-pituitary-gonad axis
Zhang H et al. 2012	Mouse	CD-1	Oral exposure	Gestational exposure: GD12.5-PND18.5	0, 0.2, 0.04, 0.08mg/kg	GD15.5, 17.5, 19.5 PND3, 5, 7	Inhibits meiosis, impairs germ cell nest breakdown
Zhang X et al. 2012	Mouse	CD-1	Oral exposure	Gestational exposure: GD0.5-PND0	0, 40, 80, 160µg/kg	PND0	Altered methylation and expression of imprinting genes
Zhou et al. 2008	Rat	Sprague-Dawley	*In vitro:* Isolated follicular cells	72 hours	10^{-4} to 10^{-7}M	30 days old	Altered steroidogenic enzyme expression and steroidogenesis
Ziv-Gal et al. 2013	Mouse	C57BL/6	*In vitro*: Antral follicles	96 hours	0.004 to 438µM	54-58 days old	Inhibited follicle growth, inhibited estradiol levels

AGD=anogenital distance; ESR1=estrogen receptor 1; F1=first filial generation; GD=gestation day; GV=germinal vesicle; GVBD=germinal vesicle breakdown; NA=not applicable; PND=postnatal day

Table S2. BPA and female human reproductive outcomes.

Source	Study design	Study population	Sample size	Timing of BPA measurement	BPA concentration (mean, geometric mean or median)	Outcome	Comments/limitations
Bloom et al. 2011a	Cross-sectional	Women undergoing IVF (University of California-San Francisco)	44	Preconception (day of egg retrieval)	Median: 2.53ng/mL serum (unconjugated)	Negative association of BPA with peak estradiol (β -0.16, 95% CI: -0.32, 0.01); null association with # oocytes retrieved (aRR: 0.95, 95% CI: 0.827, 1.10)	Small sample size, BPA measured once per treatment cycle
Bloom et al. 2011b	Prospective cohort	Couples undergoing IVF (University of California-San Francisco)	27 couples (36 women)	Preconception (day of egg retrieval)	Median: 3.3ng/ml (women) 85% detection rate vs. 0.48ng/mL (men) 53% detection rate, serum (unconjugated)	Negative association between male BPA and embryo quality (aOR: 0.54, p = 0.009) and normal embryo cleavage rate (aOR: 0.70, p = 0.07); null association of female BPA and embryo quality	Small sample size, BPA measured once, larger than expected difference in median serum BPA in men and women
Buck Louis et al. 2013	Matched cohort	Women undergoing laparoscopy/laparomy	495 individuals in operative cohort and 131 women in population cohort	At the time of laparoscopy/ screeing for endometriosis	Geometric mean for operative cohort: 1.45 (1.14-1.84) ng/ml for women with endometriosis and 1.66 (1.40-1.97) ng/ml for women without endometriosis; geometric mean for population cohort: 4.19 (2.18-8.03) ng/ml for women with endometriosis and 1.65 (1.23-2.23) ng/ml for women without endometriosis	Null association between BPA exposure and endometriosis (aOR: 0.96, 95% CI: 0.79, 1.19 for operative cohort; aOR: 1.68, 95% CI: 0.96, 2.92 for population cohort	Collection of urine samples across the menstrual cycle, not originally powered to examine BPA and endometriosis, short interval between measurement of BPA and diagnosis of endometriosis, exploratory analysis
Cobellis et al. 2009	Case-control	Women undergoing laparoscopy for chronic pelvic pain	69 (58 cases, 11 controls)	At the time of laparoscopy/ diagnosis of endometriosis	Mean± SD: 2.91 ± 1.74 ng/mL serum (in a subset of 15 women)	Positive association of BPA with endometriosis. BPA was detectable in 52% of women with endometriosis. No detectable BPA in controls.	Small sample size, limited information on exposure and confounders

Source	Study design	Study population	Sample size	Timing of BPA measurement	BPA concentration (mean, geometric mean or median)	Outcome	Comments/limitations
Ehrlich et al 2012a	Prospective cohort	Women undergoing IVF (Massachusetts General Hospital)	137 (180 IVF cycles)	Preconception (day of egg retrieval and start of cycle)	Median: 1.53 ng/mL urine (specific gravity-adjusted)	Positive linear dose response association between BPA and implantation failure (aOR: 1.02, 1.60 and 2.11 for BPA quartiles 2, 3 and 4 compared to quartile 1 (p-trend = 0.06)	Not adjusted for male BPA exposure or semen quality, BPA measured twice per treatment cycle
Ehrlich et al. 2012b	Prospective cohort	Women undergoing IVF (Massachusetts General Hospital)	174 (237 IVF cycles)	Preconception (day of egg retrieval and start of cycle)	Median: 1.50ng/mL urine (specific gravity-adjusted)	Negative association of female BPA with peak estradiol: mean decrease of 40, 253 and 471 pg/ml (p-trend 0.001); mean number of retrieved oocytes, mature and normally fertilized oocytes decreased by 24% to 27% respectively for highest vs. lowest BPA quartile (p-trend = 0.002); trend in decreased blastocyst formation (p-trend = 0.08)	Not adjusted for male BPA exposure or semen quality, BPA measured twice per treatment cycle
Ehrlich et al. 2013	Subset of ongoing prospective cohort	Women undergoing IVF (Massachusetts General Hospital)	61 women (76 IVF cycles)	Preconception (day of egg retrieval and start of cycle)	Median: 2.59 ug/L for early cycle (day 3-9) and 1.97 ug/L for the retrieval day urine	Possible U-shaped association of BPA with mean Cyp19 expression: β estimate (95% CI) for quartiles 2, 3, and 4 compared to lowest quartile: -0.97 (-2.22, 0.28), -0.97 (-2.18, 0.24), and -0.38 (-1.58, 0.82)	Limited sample size, unknown if urinary BPA levels reflects BPA levels at the ovarian follicle, timing of urine sample may not reflect relevant biological window of exposure

Source	Study design	Study population	Sample size	Timing of BPA measurement	BPA concentration (mean, geometric mean or median)	Outcome	Comments/limitations
Fujimoto et al. 2011	Cohort	Women undergoing ICSI (University of California-San Francisco)	58 infertile female and 37 male partners undergoing IVF	Preconception (day of egg retrieval)	Median: 2.53 ng/mL (women); 0.34 ng/mL (men) serum (unconjugated)	Null association between female BPA and oocyte maturation (aRR: 1.01, 95% CI: 0.98, 1.05). In 9 Asian women, significantly decreased oocyte maturation for a doubling of BPA (aRR: 0.91, 95% CI: 0.83, 1.00). Negative association of female BPA with fertilization (aRR: 0.45, 95% CI 0.21, 0.66)	Small sample size, single serum BPA, timing of male exposure not clear, larger than expected difference in median serum BPA in men and women
Galloway et al. 2010	Cross-sectional	Premenopausal women (INChianti cohort, Italy)	61	Random day of menstrual cycle	Geometric mean: 3.25 ng/mL (3.04–3.47) urine (creatinine-adjusted)	Null association of BPA with estradiol (β = - 0.026, 95% CI: -0.066, 0.014), null association with total testosterone; positive association with SHBG (β = 0.029, 95% CI: 0.004, 0.054)	Small sample size, single urine BPA estradiol measured at non-specified time during menstrual cycle
Kandaraki et al. 2011	Case-control	PCOS clinic cases and gynecology controls (Greece)	171 (71 cases PCOS; 100 controls)	At time of diagnosis of PCOS, follicular phase	Mean ± SD: 1.05±0.56 ng/mL (PCOS) vs. 0.72±0.37 ng/mL [controls (p value<0.001)] serum	Positive association of BPA with PCOS (r = 0.497, p <0.05) for all PCOS cases vs. controls and also after stratifying by lean and obese phenotypes	Cases and controls matched by age and BMI, serum BPA by ELISA (sub-optimal)
Lee SH et al. 2013	Case-control	Girls experiencing precocious puberty	114 (82 cases; 32 controls)	Childhood (7-10yr at regular checkup)	Mean ± SD: peripheral-precocious puberty, 8.7 ± 7.6μg/g creatinine; central-precocious puberty, 8.0 ± 9.9μg/g creatinine; controls, 6.6 ± 7.3μg/g creatinine urine	Null association of BPA with precocious puberty. No differences in steroid metabolism between girls with and without precocious puberty, but possible positive association between BPA levels and testosterone, estradiol and pregnenolone in all subjects.	Cases and controls matched by age, urine BPA by GC-MS, small sample size

Source	Study design	Study population	Sample size	Timing of BPA measurement	BPA concentration (mean, geometric mean or median)	Outcome	Comments/limitations
Mok-Lin et al. 2010	Prospective cohort	Women undergoing IVF (Massachusetts General Hospital)	84 (112 IVF cycles)	Preconception (day of egg retrieval and start of cycle)	Median: 2.53ng/mL urine (specific gravity-adjusted)	Negative association of BPA with peak estradiol and oocyte yield with 213pg/ml ($p = 0.03$) decrease in estradiol, and 12% ($p = 0.007$) decrease in number of oocytes retrieved per log unit increase in BPA	Small sample size, no adjustment for male exposure or semen quality, BPA measured twice per treatment cycle
Qiao et al. 2010	Case-control	Girls with and without precocious puberty	110 girls with precocious puberty and 100 girls without precocious puberty	At time of estradiol, ovary, and uterine measurements	Detected in 40.9% of precocious girls and 2% of controls	Positive association with volume of the uterus ($r = 0.557$, $p < 0.05$) and volume of the ovary ($r = 0.469$, $p < 0.01$) in precocious girls	Small sample size, no longitudinal data
Wolff et al. 2008a	Cross-sectional	9 year old girls (inner city New York city 1996-1997)	192	At time of pubertal assessment in childhood	Geometric mean: 0.24 vs. 0.11μg/g creatinine for breast stage 1 vs. 2; 0.19 vs. 0.10 μg/g creatinine for pubic hair stage 1 vs. 2	Null association of BPA with breast development (PR: 0.96, 95% CI: 0.92, 1.01) and pubic hair growth (PR: 0.98, 95% CI: 0.89, 1.08)	Cross-sectional study
Wolff et al. 2008b	Prospective cohort	Mother-infant pairs	404	Mainly third trimester of pregnancy (25% of samples collected between 25-30 weeks, 45% between 31-35 weeks, and remainder between 36-40 weeks)	Range : 0.7-35.2 μL	Null association of BPA with birth weight, birth length, head circumference, and gestational age	One measure of BPA during third trimester
Wolff et al. 2010	Prospective cohort	6-8 year old girls (multicenter: NYC, Cincinnati, California, 2004-2007)	1151	Childhood (6-8yr at baseline visit)	Median : 2.0 ng/ mL urine (creatinine-adjusted)	Null association of BPA with early onset of pubertal development (p-trend = 0.53)	One measure of BPA at baseline –1 year before reassessment of puberty development

aOR=adjusted odds ratio; aRR=adjusted relative risk; CI=confidence interval; ELISA=enzyme-linked immunoabsorbant assay; GC-MS=gas chromatography-mass spectrometry; ICSI= intracytoplasmic sperm injection; IVF=*in vitro* fertilization; PCOS=polycystic ovarian syndrome

Table S3. BPA and uterine outcomes in experimental studies.

Source	Animal	Strain	Exposure route	Time of exposure	Doses	Age at collection	Outcome
Aghajanova et al. 2011	Human	NA	*In vitro*: Endometrial stromal fibroblasts	48 hours	5-100μmol/L	NA	Decreased steroidogenic gene expression
Aldad et al. 2011	Non-human primate	African green monkey	Alzet minipump	Postnatal exposure: 28 days	50μg/kg	Adult	Decreased progesterone receptor expression
Aldad et al. 2011	Non-human primate	African green monkey	*In vitro*: Ishikawa cells	24 hours	1μM	Adult	Decreased progesterone receptor expression
An et al. 2013	Rat	Sprague-Dawley	Subcutaneous injection	Neonatal exposure: PND17-PND19	10, 100, 500mg/kg	PND20	Decreased contractile activity
Benachour and Aris 2009	Human	NA	*In vitro*: Cytotrophoblasts	24 hours	0.0002- 200μg/mL	After 24h of culture	Increased apoptosis and necrosis, induced AK activity and *Tnfα* gene and protein expression
Berger et al. 2008	Mouse	CF-1	Subcutaneous injection	Gestational exposure: GD1-GD4	0.01-300mg/kg	GD6	Decreased number of implantation sites, decreased progesterone
Berger et al. 2008	Mouse	CF-1	Subcutaneous injection	Gestational exposure: GD0,1, or 2	200 and 300mg/kg	GD6	Decreased number of implantation sites, decreased progesterone
Berger et al. 2010	Mouse	CF-1	Subcutaneous injection	Gestational exposure: GD1-GD4	100, 200, 300mg/kg	GD6	Increased luminal epithelial cell height, altered estrogen receptor and progesterone receptor gene expression
Bosquiazzo et al. 2010	Rat	Wistar	Subcutaneous injection	Neonatal exposure: PND1,3,5,7	0.05 and 20mg/kg	PND94	Decreased endometrial proliferation, decreased *Vegf* expression
Bredhult et al. 2009	Human		*In vitro*: Endometrial epithelial cells	24 hours	50μM	After 24h of culture	Decreased endometrial epithelial cell proliferation
Bromer et al. 2010	Mouse	CD-1	Intraperitoneal injection	Gestational exposure: GD9-GD16	5mg/kg	2 or 6 weeks old	Decreased methylation of *Hoxa10* promoter

Source	Animal	Strain	Exposure route	Time of exposure	Doses	Age at collection	Outcome
Hiyama et al. 2011	mouse	ICR	Subcutanous injection	Gestational exposure: GD12-GD16	100-1000mg/kg	F1 and F2: 8 weeks	Increased uterine luminal space. decreased uterine epithelium, decreased methylation of *Hoxa10* intron
Mendoza-Rodriquez et al. 2011	Rat	Wistar	Drinking water	Gestational and neonatal exposure: GD6-PND21	10mg/L (1.2mg/kg)	7 weeks old	Increased uterine stroma and epithelium thickness, decreased uterine epithelial apoptosis
Morice et al. 2011	Human	NA	*In vitro*: JEG-3 trophoblast cells	24-72h	10^{-5}M to 10^{-10}M	4-8 week placental cells	Decreased cell proliferation. Increased apoptosis
Newbold et al. 2009	Mouse	CD-1	Subcutaneous injection	Gestational exposure : GD9-16	0, 0.1, 1, 10, 100, 1000µg/kg	18months old	Increased uterine abnormalities
Salian et al. 2009a	Rat	Holtzman	Subcutaneous injection	Neonatal exposure (males only): PND1-PND5	100-1600µg/kg	PND15, 30, 45, 90	Increased fetal resorption, increased pre-implantation loss, decreased litter size
Salian et al. 2009b	Rat	Holtzman	Oral gavage	Gestational and neonatal exposure (males only): GD12-PND21	1.2 and 2.4µg/kg	GD20 or PND125	Increased fetal resorption, decreased litter size, increased hormone imbalances
Signorile et al. 2010	Mouse	Balb-c	Subcutaneous injection	Gestational exposure : GD1-PND7	100 and 1000µg/kg	3 months old	Increased endometriosis-like structures
Susiarjo et al. 2013	Mouse	C57BL/6 Cast7	Dietary exposure	Gestational exposure: Prebreed to GD9.5	10µg/kg and 10mg/kg	F1: GD9.5	Disrupted imprinted gene expression in embryos and placenta
Tan et al. 2013	Mouse	ICR	Oral gavage	Gestational exposure : GD13-GD16	2, 20, 200mg/kg	GD17	Activated protein kinase C signaling
Tiwari and Vanage 2013	Rat	Holtzman	Oral gavage	Postnatal exposure (males only): 6 days	5 and 10µg/kg	GD15 (untreated female mated to treated male)	Decreased implantation sites, increased resorption sites

Source	Animal	Strain	Exposure route	Time of exposure	Doses	Age at collection	Outcome
Varayoud et al. 2008	Rat	Wistar	Subcutaneous injection	Neonatal exposure: PND 1, 3, 5, and 7	0.5 and 20mg/kg	PND8 or PND94	Decreased steroid hormone responsiveness of uterine stroma, decreased *Hoxa10* and *Hoxa11* expression
Varayoud et al. 2011	Rat	Wistar	Subcutaneous injection	Neonatal exposure: PND1, 3, 5, and 7	0.05 and 20mg/kg	F1: GD5 or GD18	Decreased implantation sites, decreased implantation-regulating gene expression
Xiao et al. 2011	Mouse	C57BL/6	Subcutaneous injection	Gestational exposure: GD0.5-GD3.5	0, 0.025, 0.5, 10, 40, 100mg/kg	GD4.5 or GD5.5	Ablated implantation, decreased embryo transport
Yigit and Daglioglu 2010	Chicken	White Leghorn	In ovo injection	Incubation day 4	67 and 134µg/g	21 weeks old	Decreased hatching proportion, uterine tubular glandular density, and thickness of tunica mucosa

AK=adenylate kinase; GD=gestation day; HOXA=homeobox A; GD=gestation day; PND=postnatal day; Tnfa=tumor necrosis factor alpha; vegf=vascular endothelial factor

Table S4. BPA and human pregnancy and birth outcomes.

Source	Study design	Study population	Sample Size	Timing of BPA measurement	BPA concentration (mean, geometric mean or median)	Outcome	Comments/limitations
Cantowine et al. 2010	Nested case-control in a prospective cohort	Pregnant women Mexico city (ELEMENT cohort)	60 (12(20%) preterm births)	Third trimester archived spot urine samples	Geometric mean: 1.45ng/mL for all women; 1.94ng/mL for women delivering preterm. Urine (SG- adjusted)	Borderline positive BPA association with preterm birth, (OR 1.91, 95% CI: 0.93, 3.91)	Pilot study, small sample size
Chou et al. 2011	Cross-sectional	Taiwanese mothers and infants	97	At delivery	Geometric mean: 2.5ng/mL (maternal serum); 0.5ng/mL (neonatal cord blood)	Positive association of BPA with low birth weight (OR 2.42, 95% CI: 1.72, 3.36); small for gestational age (OR 2.01, 95% CI: 1.39, 3.01); high leptin (OR 1.67, 95% CI: 1.12, 2.25); and low adiponectin (OR 1.25, 95% CI: 1.52, 3.97)	Small sample size, cross sectional design
Fenichel et al. 2012	Matched case-control	Boys with cryptorchidism (France)	152 (46 cases; 106 controls)	Cord blood at birth	Median: 0.86ng/mL in controls); 0.92ng/mL in cases serum (unconjugated)	Null association of BPA with cryptorchidism. However, significant positive correlation with testosterone and inhibin B levels	Exposure assessment of maternal BPA during pregnancy is important given the short half -life of BPA
Lee BE et al. 2013	Multi-center birth cohort	Korean mothers and children	757	Third trimester	Geometric mean: 1.29μg/L (1.87μg/g creatinine) during late pregnancy	Positive association between BPA levels and birth weight; second tertile of maternal BPA exposure exhibited an increase in birth weight relative to the first tertile ($p = 0.04$)	Urine levels of BPA may not reflect circulating levels, used spot urines. BPA values normalized to creatinine only
Miao et al. 2011a	Occupational cohort retrospective	Children of occupationally exposed Chinese parents	587	Exposure history and personal air sampling, job/exposure matrix; current urine in a subgroup, but not for index pregnancy	Geometric mean: Exposed mothers (direct exposure): 15.98μg/g Cr (N=50). Spouses of exposed men (indirect): 2.22μg/g Cr (N=93). Unexposed mothers: 0.56μg/g Cr (N=444) urine (cr-adjusted)	Negative association of BPA with birth weight ($\beta = -168$g, $p = 0.02$) for directly exposed fetus (maternal exposure); ($\beta = -91$g, $p = 0.10$) for indirectly exposed fetus (father exposed during pregnancy)	30-50% of women had their index pregnancy over 15 years prior to enrollment to the study, exposure was partly estimated using exposure history of occupational exposure, self-report of baby's birth weight. possible recall bias exists due elapsed time

Source	Study design	Study population	Sample Size	Timing of BPA measurement	BPA concentration (mean, geometric mean or median)	Outcome	Comments/limitations
Miao et al. 2011b	Occupational cohort study retrospective	Children of occupationally exposed parents (age 0-17 years)	153 (106 controls, 46 cases)	Personal air sampling at time of index pregnancy, current urine for different categories of exposure as defined using occupational history and job/exposure matrix	Geometric mean: Exposed mothers (direct exposure): 16.0 μg/g Cr (N=18). Spouses of exposed men (indirect): 2.2μg/g Cr (N=38). Unexposed mothers: 0.6μg/g Cr(N=97) Urine (cr-adjusted)	Positive linear dose response association of BPA with shortened AGD in boys by level of exposure, p-trend = 0.008; in boys of exposed mothers, decrease in AGD of 8.11mm (p = 0.003) and 2.87mm (p = 0.15) in boys of exposed fathers during index pregnancy	Wide age range of children at time of AGD measurement. Almost 20% of boys were older than 10 years. Uncertain generalizability to the environmentally exposed population
Padmanabhan et al. 2008	Cross-sectional	Southeastern Michigan mothers	40	At delivery	Mean (SEM): 5.9 (0.94) ng/mL serum (unconjugated)	Null association of BPA with birth weight and gestational length. Mothers with maternal BPA concentrations less than or equal to 5ng/ml had babies with similar birth weight to mothers with maternal BPA concentrations above 5ng/mL	Small sample size, limited information on exposure by birthweight (cut-off of 5ng/mL used in analyses), single spot serum at delivery
Philippat et al. 2012	Nested case-control	Mother-infant male pairs (France)	191	6-30 weeks gestation	Median: 3.1ng/mL (in mother) urine	Suggestive inverted U-shape association between BPA and birth weight in tertile analysis 169g (95% CI: 14, 324); 85g (-62, 233) for tertile 2 and 3, respectively. Increase in head circumference by 0.3cm (95% CI: 0.0, 0.7)	Single spot urine sample at one time point during pregnancy
Snijder et al. 2013	Prospective cohort study	Pregnant Dutch women	219	Early, mid, and late pregnancy	Geometric mean (SEM): 3.2 (2.3) μg/g creatinine	Negative association of BPA with fetal growth and head circumference. Among 80 women with three BPA measurements, women with BPA levels above 4.22μg/g creatinine had lower fetal growth rates and fetuses with smaller head circumference than women with BPA levels less than 1.54μg/g creatinine.	Small sample size, difficult to obtain solid estimate of first trimester fetal growth

Source	Study design	Study population	Sample Size	Timing of BPA measurement	BPA concentration (mean, geometric mean or median)	Outcome	Comments/limitations
Wolff et al. 2008b	Prospective cohort	Mother-infant pairs	404	Mainly third trimester of pregnancy (25% of samples collected between 25-30 weeks, 45% between 31-35 weeks, and remainder between 36-40 weeks)	Range : 0.7-35.2μL	Null association of BPA with birth weight, birth length, head circumference, and gestational age	One measure of BPA during third trimester

AGD=anogenital distance; CI=confidence interval; Cr=creatinine; OR=odds ratio; SEM=standard error of the mean; SG=specific gravity

Table S5. BPA and pregnancy outcomes in experimental studies.

Source	Animal	Strain	Exposure route	Time of exposure	Doses	Age at collection	Outcome
Cabaton et al. 2011	Mouse	CD-1	Alzet pump	Gestational exposure: GD8-PND16	25ng, 250ng, 25µg/kg	2-8months old	Decreased number of pregnancies, decreased number of pups
Howdeshell et al. 2008	Rat	Long-Evans	Oral gavage	Gestational exposure: GD7-PND18	2, 20, 200µg/kg	PND150	No adverse effects on pregnancy outcomes
Kobayashi et al. 2010	Mouse	C57BL/6	Dietary exposure	Gestational, neonatal, and postnatal exposure: F1: GD6-PND22; postnatal until sacrifice	0.05, 0.5, 5.0mg/kg	F1: 13 weeks	No adverse effects on pregnancy outcomes
Kobayashi et al. 2010	Mouse	C57BL/6	Dietary exposure	Gestational, neonatal, and postnatal exposure: F2: GD6-PND22; postnatal until sacrifice	0.05, 0.5, 5.0mg/kg	F2:15 weeks	No adverse effects on pregnancy outcomes
Kobayashi et al. 2012	Rat	Sprague-Dawley	Dietary exposure	Gestational and neonatal exposure: GD6-PND21	0.05, 0.5, 5.0mg/kg	5weeks; 3 months	No adverse effects on pregnancy outcomes
Nah et al. 2011	Mouse	ICR	Subcutaneous injection	Neonatal exposure: PND8	0.1, 1, 10, 100mg/kg	PND20-PND29; PND25, 30, 70	Decreased pup weight
Nanjappa et al. 2012	Rat	Long-Evans	Oral gavage	Gestational exposure: GD12-PND21	2.5 and 25µg/kg	PND90	No adverse effects on pregnancy outcomes
Ryan BC et al. 2010	Rat	Long-Evans	Oral gavage	Gestational and neonatal exposure: GD7-PND18	2, 20, 200µg/kg		No adverse effects on pregnancy outcomes
Salian et al. 2009a	Rat	Holtzman	Subcutaneous injection	Neonatal exposure (males only): PND1-5	100-1600µg/kg	PND15, 30, 45, 90	Decreased number of pups
Salian et al. 2009b	Rat	Holtzman	Oral gavage	Gestational exposure (males only): GD12-PND21	1.2 and 2.4µg/kg	Males: PND125 Females: GD20	Decreased number of pups
Tan et al. 2013	Mouse	ICR	Oral gavage	Gestational exposure: GD13-GD16	2, 20, 200mg/kg	GD17	Placenta gene changes that could cause pre-term birth
Thuillier et al. 2009	Rat	Sprague-Dawley	Oral gavage	Gestational exposure: GD14-PND0	0.1 to 200mg/kg	PND 3, 21, 60	No adverse effects on pregnancy outcomes
Tyl et al. 2008	Mouse	CD-1	Dietary exposure	Gestational exposure: F0 8 weeks pre-breed, GD1-GD14	0.003, 0.03, 0.3, 5, 50, 600mg/kg	PND1/birth	Increased pup weight

Source	Animal	Strain	Exposure route	Time of exposure	Doses	Age at collection	Outcome
Tyl et al. 2008	Mouse	CD-1	Dietary exposure	Postnatal exposure: F1:8 weeks pre-breed	0.003, 0.03, 0.3, 5, 50, 600mg/kg	PND1/birth	Increased pup weight
Xi et al. 2011	Mouse	CD-1	Oral gavage	Postnatal exposure: F0: GD1-PND20	12, 25, 50mg/kg	PND50	No adverse effects on pregnancy outcomes
Xi et al. 2011	Mouse	CD-1	Oral gavage	Postnatal exposure: F1: PND21-PND49	12, 25, 50mg/kg	PND50	No adverse effects on pregnancy outcomes
Xi et al. 2011	Mouse	CD-1	Oral gavage	Postnatal exposure: F1: PND21-49	12, 25, 50mg/kg	PND50	No adverse effects on pregnancy outcomes
Yigit and Daglioglu 2010	Chicken	White Leghorn	In ovo injection	Incubation day 4	67 and 134µg/g	21 weeks old	Decreased hatching

F0=parental generation; F1=first filial generation; GD=gestation day; PND=postnatal day

Table S6. BPA and male human reproductive outcomes.

Source	Study design	Study population	Sample Size	Timing of BPA measurement	BPA concentration (mean, geometric mean or median)	Outcome	Comments/limitations
Galloway et al. 2010	Cross-sectional	Italian adults between 20-74 years of age (INChianti)	715	Adulthood, same day as testosterone measure	Geometric mean: 4.02ng/mL (3.76–4.31) urine (creatinine-adjusted)	Positive association of BPA with total testosterone ($\beta = 0.05$, 95% CI: 0.02, 0.08), no association with sex hormone binding globulin and free testosterone	Relatively high BPA concentration for general population, cross-sectional study design, spot urine sample
Li DK et al. 2010	Cross-sectional	Occupationally exposed men from 4 regions of China	427	Pre and post shift	Median : 53.7μg/g creatinine (occupationally exposed) and 1.2μg/g Cr (unexposed) urine (creatinine-adjusted)	Positive association of BPA with sexual dysfunction, decreased sexual desire ($\beta = 0.016$, $p < 0.001$), erectile dysfunction ($\beta = 0.022$, $p < 0.001$), orgasmic function ($\beta = -0.017$, $p < 0.001$), and overall satisfaction with sex life ($\beta = -0.010$, $p = 0.003$)	Self-reported sexual dysfunction, low participation rate, possible current co-exposures
Li DK et al. 2011	Prospective cohort study	Occupationally exposed Chinese men	218	Pre and post shift	Median: 38.7ng/mL (occupationally exposed) and 1.4ng/mL (unexposed) urine (creatinine-adjusted)	Negative linear association of BPA with sperm concentration ($\beta = 15.6$, $p < 0.001$); sperm count ($\beta = -42.1$, $p = 0.004$) and increased odds of decreased sperm motility (OR: 2.3, 95% CI: 1.0, 5.1). Associations stronger after excluding occupationally exposed men.	Only two semen samples collected at 1-3 week intervals, small sample size for sub-analysis on men not occupationally exposed to BPA (N=88), uncertain generalizability to men exposed to environmentally relevant BPA concentrations
Meeker et al. 2010a	Cross-sectional	Male partners of couples seeking treatment for subfertility (Massachusetts General Hospital)	190	Same day as semen sample collection (additional urine samples for a subgroup collected weeks to months prior to semen sample)	Median: 1.3ng/mL urine (specific gravity-adjusted)	Negative association of BPA with sperm concentration: -23% (95% CI: -40%, -0.3%), morphology: -13% (95% CI: -26%, -0.1%), suggestive decrease in sperm motility: -7.5% (95% CI: -17%, 1.5%), and increase in sperm DNA damage: 10% (95% CI: 0.03%, 19%)	Associations only observed when semen parameters were modeled on a continuous scale, but not when modeled as binary outcome, uncertain generalizability of results to men from general population

Source	Study design	Study population	Sample Size	Timing of BPA measurement	BPA concentration (mean, geometric mean or median)	Outcome	Comments/limitations
Meeker et al. 2010b	Cross-sectional	Male partners of couples seeking treatment for subfertility (Massachusetts General Hospital)	167	Same day as blood sample for hormone measurements. Repeat samples in 75 men up to 2.5 months later	Median: 1.3ng/mL urine (specific gravity-adjusted)	Negative association of BPA with estradiol:testosterone ratio (β = 0.86, p = 0.01) and free androgen index (β = 0.89, p = 0.02), and positively associated with FSH (β = 1.18, p = 0.01) and FSH:inhibin B ratio (β = 1.28, p = 0.05)	Cross sectional study design, megative association with estradiol:testosterone ratio was consistent when modeling repeat urine BPA concentrations, but only a limited number of repeat samples were available, generalizability to men of general population is uncertain
Mendiola et al. 2010	Cross-sectional	Fertile male partners of pregnant women (Multicenter: Study for Future Families)	302 men (hormones) 317 men (semen quality)	Same day as hormone profile and semen collection	Median: 1.7 ng/mL urine (unadjusted) creatinine-adjusted	Positive association of BPA with sex hormone binding globulin (β = 0.07, 95% CI: 0.007, 0.13). Negative association with free androgen index (β = -0.01, 95% CI: -0.09, -0.004) and free androgen index: luteinizing hormone ratio (β = -0.11, 95% CI: -0.18, -0.03). Null associations with semen quality parameters.	Cross sectional study design

CI=confidence interval; Cr= creatinine; FSH=follicle-stimulating hormone; OR=odds ratio

Table S7. BPA and male reproductive outcomes in experimental studies.

Source	Animal	Strain	Exposure route	Time of exposure	Doses	Age at collection	Outcome
Arase et al. 2011	Mouse	C57BL/6	Oral gavage	Gestational exposure: GD13-GD16	20µg/kg	GD17 to PND1	Increased estradiol levels, increased steroidogenic enzyme expression in urogenital sinus
Anjum et al. 2013	Mouse	Swiss albino	Oral exposure	Postnatal exposure: adult	10mg/kg body weight	Adult, exact age unknown, after 14 days of dosing	Increased oxidative stress in testes
Castro et al. 2013	Rat	Wistar	Subcutaneous injection	Postnatal exposure: adult (4 days)	25, 50, 300, and 600µg/kg	Adult (exact age not reported, 30 min after last injection)	Decreased testosterone, increased estradiol
D'Cruz et al. 2012a	Rat	Wistar	Oral gavage	Postnatal exposure: 90-135 days old (45 days)	0.005, 0.5, 50, 500µg/kg	136 days old	Decreased expression of glucose transporters, increased reactive oxygen species production
D'Cruz et al. 2012b	Rat	Wistar	Oral gavage	Postnatal exposure: 90-135 days old (45 days)	0.005, 0.5, 50, 500µg/kg	136 days old	Decreased insulin signaling, decreased glucose transport, decreased steroidogenic enzymes. decreased testosterone
De Flora et al. 2011	Rat	Sprague-Dawley	Drinking water	Postnatal exposure: adult (10 days)	200mg/kg	Adult (exact age not reported, 24h after last exposure day)	Increased sperm DNA fragmentation, increased DNA adducts in prostate, increased clusterin expression
Dobrzynska and Radzikowska 2013	Mouse	Pzh:SFIS	Drinking water	Postnatal exposure: 8-10 weeks (14 days)	5, 10, 20, 40mg/kg	10 weeks old	Decreased sperm count and motility, increased abnormal morphology of sperm, induced sperm DNA strand breaks
El-Beshbishy et al. 2012	Rat	Albino	Oral exposure	Postnatal exposure: adult (14 days)	10mg/kg	Adults (exact age not reported, after last exposure day)	Decreased testes weight and protein content, decreased antioxidant enzymes, decreased glutathione content, increased lipid peroxidation, decreased testosterone
Fang et al 2013	Mouse	Kunming	Oral gavage	Postnatal exposure: 4-5 weeks	0.5mg/kg body weight	3 weeks after last dose	Increased oxidative stress, decreased testes weight, decreased testosterone

Source	Animal	Strain	Exposure route	Time of exposure	Doses	Age at collection	Outcome
Horstman et al. 2012	Rat	Sprague-Dawley	Subcutanous exposure	Gestational exposure: GD11-GD20	0.02, 0.5, 400mg/kg	F1: GD16, 18, or 20	Decreased *Star* expression and protein levels
Howdeshell et al. 2008	Rat	Long-Evans	Oral gavage	Gestational and postnatal exposure: GD7-PND18	2, 20, and 200µg/kg	PND150	No change in reproductive organ weight, no effect on AGD
Jin et al. 2013	Rat	Sprague-Dawley	Oral gavage	Postnatal exposure: 12-14 weeks (14 weeks)	2 µg/kg	14 weeks old	Decreased hormone production, decreased sperm and germ cell count, no change in testis weight, increased apoptosis
Kobayashi et al. 2010	Mouse	C57BL/6	Dietary exposure	Gestational, neonatal, and postnatal exposure: GD6-PND22; postnatal until sacrifice	0.05, 0.5, 5.0mg/kg	13 or 15 weeks old	Reduced sperm motility, no change in sperm count, AGD, or reproductive organ weight
Kobayashi et al. 2012	Rat	Sprague-Dawley	Dietary exposure	Gestational and neonatal exposure: GD6-PND21	0.017, 0.17, 1.7mg/kg	5 weeks or 3 months old	No change in hormones, sperm count/motility, AGD, testis, or prostate weight
LaRocca et al. 2011	Mouse	C57BL/6	Oral gavage	Gestational exposure: GD10-GD16	50 and 1000µg/kg	PND56	No effect on spermatogenesis, Sertoli cell gene expression, serum testosterone levels, or AGD
Li Y et al. 2009	Mouse	Kunming	Oral gavage	Postnatal exposure: PND31-PND44	160, 480, 960mg/kg/d	PND 45, 60, 90	Increased germ cell apoptosis, Leydig cell apoptosis, decreased spermatogenesis, increased FasL signaling
Liu et al. 2013	Rat	Wistar	Oral gavage	Postnatal exposure: 9-18 weeks old (60 days)	2, 20, 200µg/kg	18 weeks old	Decreased sperm counts, inhibited spermiation, persistent meiotic DNA strand breaks, increased germ cell apoptosis
Minamiyama et al. 2010	Rat	Wistar	Drinking water	Postnatal exposure: 8-16 weeks old (56 days)	1.0 or 10mg/L	16 weeks old	No change in sperm count, reduced sperm motility, increased production of ROS in sperm
Minamiyama et al. 2010	Rat	Wistar	Drinking water	Postnatal exposure: 12 weeks old (7 days)	1.0mg/L	12 weeks old	No change in sperm count, reduced sperm motility, increased production of ROS in sperm

Source	Animal	Strain	Exposure route	Time of exposure	Doses	Age at collection	Outcome
Nakamura et al. 2010	Rat	Wistar/st	Subcutaneous injection	Postnatal exposure: 4-9 weeks old (4 days a week for 6 weeks)	20, 100, 200mg/kg (11.4, 57.1, 114.2 mg/kg/day)	9 weeks old	Decreased serum and intratesticular testosterone, decreased steroidogenic enzyme expression, decreased *Esr1* expression, decreased Leydig cell number, decreased LH
Nanjappa et al. 2012	Rat	Long-Evans	Oral gavage	Gestational and neonatal exposure: GD12-PND21	2.5 and 25µg/kg	PND 21.35, 90	Increased Leydig cell number, decreased Leydig cell testosterone production, increased LHR, ESR1, AR
N'Tumba-Byn et al. 2012	Human	NA	*In vitro:* Fetal testes	3 days	10pM-10µM	6.5-10.5 gestational weeks	Reduced testosterone and INSL3 mRNA levels
N'Tumba-Byn et al. 2012	Rat	Wistar	*In vitro:* Fetal testes	3 days	10pM-10µM	14.5 DPC	Reduced testosterone in rodent testes
N'Tumba-Byn et al. 2012	Mouse	C57BL/6	*In vitro:* Fetal testes	3 days	10pM-10µM	12.5 DPC	Reduced testosterone in rodent testes
Okada and Kai 2008	Mouse	ICR	Silastic capsule	Gestational and neonatal exposure: Pre-breed through PND28	1.2 and 60µg/day	PND 28	Reduced mature spermatids number, no change in testosterone
Prins et al. 2011	Rat	Sprague-Dawley	Subcutaneous injection	Neonatal exposure: PND1, 3, and 5	10µg/kg	28 weeks old	Increased prostate intraepithelial neoplasia incidence
Prins et al. 2011	Rat	Sprague-Dawley	Oral exposure	Neonatal exposure: PND1, 3, and 5	10µg/kg	28 weeks old	Increased prostate intraepithelial neoplasia incidence
Qiu et al. 2013	Rat	Sprague-Dawley	Oral gavage	Postnatal exposure: 9-16 weeks old (56 days)	0.0005, 0.5, 5mg/kg	16 weeks old	Altered steroidogenic enzyme expression, decreased sperm count
Rashid et al. 2013	Mouse	Swiss albino	Oral exposure	Postnatal exposure: adult	10 mg/kg body weight	Adult, exact age unknown, after 14 days of dosing	Increased oxidative stress
Salian et al. 2009a	Rat	Holtzman	Subcutaneous injection	Neonatal exposure: PND1-PND5	100-1600µg/kg	PND15, 30, 45, 90, 125	Decreased sperm count, altered hormone production
Salian et al. 2009b	Rat	Holtzman	Oral gavage	Gestational and neonatal exposure: GD12-PND21	1.2 and 2.4µg/kg	PND125	Decreased steroid receptors in F1, F2, F3
Sánchez et al. 2013	Rat	Wistar	Subcutaneous injection	Postnatal exposure: adult (4 days)	25 and 300µg/kg	30 min after last treatment	Decreased DHT levels, no effect on testosterone levels, decreased expression of *5αR1* and *5αR2*

Source	Animal	Strain	Exposure route	Time of exposure	Doses	Age at collection	Outcome
Tainaka et al. 2012	Mouse	ICR	Subcutaneous injection	Gestational exposure: GD7 and GD14	5 and 50mg/kg	F1: 6 weeks old	Decreased sperm count, gene expression mediating spermatozoa, altered Sertoli cell number and morphology, decreased genes mediating Sertoli cell function and androgen signaling
Tang et al. 2012	Rat	Sprague-Dawley	Subcutaneous injection	Neonatal exposure: PND1, 3, and 5	10μg/kg	PND10, 90, 200	Altered methylation and expression of genes and transcriptional proteins in prostate
Thuillier et al. 2009	Rat	Sprague-Dawley	Oral gavage	Gestational exposure: GD14-PND0	0.1-200mg/kg	PND 3, 21, 60	Transient alterations in the MAPK signaling pathway
Tiwari and Vanage 2013	Rat	Holtzman	Oral gavage	Postnatal exposure: Adults (6 days)	5 and 10μg/kg	End of mating cycle (treated males; 1 to 8 weeks)	Impaired mid-spermatids and spermatocytes, decreased sperm production and motility, increased sperm DNA damage
Tyl et al. 2008	Mouse	CD-1	Dietary exposure	Gestational exposure: F0: 8 weeks pre-breed, GD1-GD14	0.003, 0.03, 0.3, 5, 50, 600mg/kg	PND1/birth	Decreased absolute AGD and delayed preputial separation, no effect on sperm, organ weight, or reproductive organ structure
Tyl et al. 2008	Mouse	CD-1	Dietary exposure	Postnatal exposure: F1: 8 weeks pre-breed	0.003, 0.03, 0.3, 5, 50, 600mg/kg	PND1/birth	Decreased absolute AGD and delayed preputial separation, no effect on sperm, organ weight, or reproductive organ structure
Wang Q et al. 2010	Mouse	CD-1	Oral gavage	Postnatal exposure: PND35-PND49	160 and 480mg/kg	PND50	Increase germ cell apoptosis, increased FasL signaling pathway, increased mitochondrial apoptotic signaling pathway
Wu et al. 2013	Rat	Sprague-Dawley	Oral gavage	Postnatal exposure: 8-10 weeks old (10 days)	200mg/kg	10 weeks old (24h after treatment)	Induced DNA damage, induced oxidative stress
Wu et al. 2011	Rat	Sprague-Dawley	Intragastric injection	Postnatal exposure: Adult (4 weeks)	10, 30, 90μg/kg	12 weeks old	Decreased testosterone

Source	Animal	Strain	Exposure route	Time of exposure	Doses	Age at collection	Outcome
Xi et al. 2011	Mouse	CD-1	Oral gavage	Gestational and neonatal exposure: F0: GD1-PND20	12, 25, 50mg/kg	PND50	Decreased steroidogenic enzyme expression, decreased testosterone
Xi et al. 2011	Mouse	CD-1	Oral gavage	Postnatal exposure: F1: PND21-PND49	12, 25, 50mg/kg	PND50	Decreased steroidogenic enzyme expression, decreased testosterone
Xi et al. 2011	Mouse	CD-1	Oral gavage	Postnatal exposure: F1: PND21-PND49	12, 25, 50mg/kg	PND50	Decreased steroidogenic enzyme expression, decreased testosterone

AGD=anogenital distance;AR=androgen receptor; DPC=days post coitum; F0=parental generation; F1=first filial generation; F2=second filial generation; F3=third filial generation; GD=gestation day; Esr1=estrogen receptor 1;Fasl=Fas ligand; INSL=insulin like factor; LH=luteinizing hormone; MAPK=mitogen activated protein kinase; PND=postnatal day; Star=steroidogenic acute regulatory protein

Table S8. BPA and sexual function outcomes in experimental studies.

Source	Animal	Strain	Exposure route	Time of exposure	Doses	Age at collection	Outcome
Adewale et al. 2009	Rat	Long-Evans	Subcutaneous injection	Neonatal exposure: PNDO-PND3	50µg/kg and 50mg/kg	PND148	Accelerated vaginal opening
DeCatanzaro et al. 2013	Mouse	CF-1	Dietary exposure	Postnatal exposure: GD10-PND9	0.175, 1.75, 17.5µg	PND60 or PND90	Increased latency to insemination, decreased intromissions with females, decreased ejaculations
DeCatanzaro et al. 2013	Mouse	CF-1	Dietary exposure	Postnatal exposure: GD10-PND9	17.5, 175, 1750µg	PND85-PND105	Increased latency to insemination, decreased intromissions with females, decreased ejaculations
Fernandez et al. 2009	Rat	Sprague-Dawley	Subcutaneous injection	Gestational exposure: PND1-10	5µg/50µL, 50µg/50µL, 500µg/50µL	PND12; adults	Accelerated puberty onset and estrous cyclicity, decreased gonadotropin releasing hormone and luteinizing hormone function
Nah et al. 2011	Mouse	ICR	Subcutaneous injection	Neonatal exposure: PND8	0.1, 1, 10, 100mg/kg	PND20-PND29; PND25, 30, 70	Accelerated vaginal onset, decreased estrous cyclicity
Ryan et al. 2010	Rat	Long-Evans	Oral gavage	Gestational and neonatal exposure: GD7-PND18	2, 20, 200µg/kg	NA	No adverse sexual function effects
Salian et al. 2009a	Rat	Holtzman	Subcutaneous injection	Neonatal exposure (males only): PND1-5	100-1600µg/kg	PND15, 30, 45, 90	Increased time taken for copulation, decreased copulation index
Salian et al. 2009b	Rat	Holtzman	Oral gavage	Gestational exposure (males only): GD12-PND21	1.2 and 2.4µg/kg	males: PND125 females: GD20	Increased time taken for copulation in F1, F2, F3

Source	Animal	Strain	Exposure route	Time of exposure	Doses	Age at collection	Outcome
Tyl et al. 2008	Mouse	CD-1	Dietary exposure	Gestational exposure: F0: 8 weeks pre-breed, GD1-GD14	0.003, 0.03, 0.3, 5, 50, 600mg/kg	PND1/birth	No adverse sexual function effects
Tyl et al. 2008	Mouse	CD-1	Dietary exposure	Postnatal exposure: F1: 8 weeks pre-breed	0.003, 0.03, 0.3, 5, 50, 600mg/kg	PND1/birth	No adverse sexual function effects

F1=first filial generation; F2=second filial generation; F3=third filial generation; GD=gestation day; PND=postnatal day

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